CASE REPORT

Nephrotic syndrome complicated with severe dengue infection in a child

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ABSTRACT

Dengue illness is characterised by plasma leakage with or without bleeding, which may lead to dengue shock syndrome. Proteinuria and hypoalbuminaemia are common in dengue infection, and few cases of heavy proteinuria have been reported. Dengue infection features may mimic nephrotic syndrome in clinical practice. As dengue infection is endemic in India, it can be associated with other illnesses such as nephrotic syndrome. We report a child with nephrotic syndrome complicated with severe dengue infection.

KEYWORDS

Nephrotic syndrome; Severe dengue infection; Proteinuria; Complication.

INTRODUCTION

Throughout the world, an estimated 50 million dengue infections occur annually [1]. The spectrum of dengue ranges from mild febrile illness to a life-threatening severe infection. Nephrotic syndrome is associated with heavy (nephrotic-range) proteinuria. Nephrotic-range proteinuria is defined as proteinuria >3.5 g/24 hours or a urine protein:creatinine ratio >2. The triad of clinical findings associated with nephrotic syndrome are oedema, hypoalbuminaemia (≤2.5 g/dl) and hyperlipidaemia (cholesterol >200 mg/dl) [2]. Dengue illness is characterised by plasma leakage with or without bleeding, which may lead to dengue shock syndrome. Proteinuria is one of the common abnormal findings detected by urine analysis in dengue infection, and few cases of heavy proteinuria have been reported [3–6]. As dengue infection is endemic in India, it can be associated with other illnesses such as nephrotic syndrome. We report a child with nephrotic syndrome complicated with severe dengue infection.

CASE REPORT

A 9-year-old boy presented with puffiness of face for 5 days, swollen feet for 2 days and fever and decreased urine output for 1 day. He also had nausea and persistent vomiting. There was no rash. There was no history of haematuria or micturition disturbances. On examination, he was febrile (temperature 39.4°C), pulse rate (PR) 98/minutes, respiratory rate (RR) 24/minutes, Blood Pressure (BP) 118/80 mm of Hg, capillary refill time (CRT) <3 seconds and oxygen saturation 98% at room air. He had puffiness of the face and bilateral pedal oedema. There was no evidence of skin or throat infection. Other system examination was unremarkable.

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On the 2nd day of admission, he was febrile, puffy and pedal oedema, and abdominal distension (ascitis) was detected. His vital signs revealed BP 114/76 mm of Hg, PR 90/minutes, RR 24/minutes, CRT <3 seconds and oxygen saturation 98% at room air.

On the 3rd day, his fever was persisting, urine output decreasing and abdominal distension increased. His vital signs showed PR 122/minutes, low volume pulse, BP 98/80 mm of Hg with narrow pulse pressure (difficulty in recording), RR 24/minutes, CRT <4 seconds and oxygen saturation 95% at room air. Therefore, a fluid challenge was given and dopamine10 µg/kg/minute started. In view of low serum albumin (1.9 g/dl), albumin infusion 1 g/kg was started. His BP improved, and maintenance intravenous fluids were given.

On the 4th day of admission, his puffiness and abdominal distension increased, scrotal oedema appeared and he became tachypnoea. His vital signs: RR 44/minutes, PR 100/minutes, low volume pulse, BP 122/100 mm of Hg (difficult to record narrow pulse pressure), CRT <3 seconds and oxygen saturation 98% with 5 l of oxygen. Respiratory examination revealed diminished air entry on the right side. A chest X-ray showed pleural effusion on the right side. Therefore, non-invasive ventilation (NIV) was started, and dobutamine and dexamethasone were added.

On the 5th day, there was generalised swelling of the body with scrotal oedema. On NIV and inotropes, his vitals were as follows: RR 36/minutes, BP of 122/84 mm of Hg and maintaining saturation of 99%. A chest X-ray showed the features of pneumonia. Therefore, injections of ceftriaxone and linezolid were started.

On the 6th day of admission, still on NIV, there was a decrease in the generalised swelling of the body. His vital signs were as follows: RR 30/minutes, PR 102/minutes, BP130/110 of Hg, CRT <3 seconds and O_2 saturation 99%. Dopamine was stopped, and we started tapering dobutamine.

On the 7th day, there was only mild swelling of the body present, and tachypnoea decreased. Vital signs were as follows: RR 28/minutes, BP 130/90 of Hg and O2 saturation 99%. Therefore, stopped NIV and dobutamine were stopped, and oxygen was started through nasal prongs.

On the 8th day, he was on oxygen through nasal prongs (2 l) and had only mild puffiness of face without scrotal oedema or abdominal distension. Vital signs were as follows: RR 24/minutes, BP 120/70 mm of Hg, PR 90/minutes and oxygen saturation 94% at room air. Chest X-ray revealed a decrease in pleural effusion and clearance of pneumonia. Antibiotics were continued. Dexamethasone was stopped, and prednisolone was added. Pneumonia was treated with antibiotics for 10 days. Nephrotic syndrome was treated with dexamethasone followed by oral prednisolone. On discharge, his serum albumin was 27 g/l and platelet count 324 × 10^9/l. His follow-up for another 6 months was uneventful without relapse.

The patient presented with a fever of 1 day, and it lasted for 3 days in the hospital. His nausea and persistent vomiting lasted for 2 days. At the same time, we had an epidemic of dengue fever. On the 3rd day of admission, he had low volume pulse, BP 98/80 mm of Hg with narrow pulse pressure (difficulty in recording) and CRT < 4 seconds. His Enzyme-Linked Immunosorbent Assay (ELISA) for dengue NS1 antigen was positive. His platelets decreased to 116 × 10^9/l from 284 × 10^9/l. Blood and urine cultures were sterile, and Weil-Felix and Widal tests were negative. Sonography revealed oedematous gall bladder and wall thickening (6 mm), moderate ascites and bilateral pleural effusion. Therefore, we diagnosed the condition as dengue shock and treated accordingly. The investigations are shown in Tables 1 and 2.

DISCUSSION

The child presented with puffiness of face for 5 days and swollen feet for 2 days followed by fever. After admission, his abdominal distension gradually increased due to ascitis along with gross scrotal oedema. He had all classical features of nephrotic syndrome including heavy proteinuria and hyperlipidaemia. His platelets started decreasing after 4th day, had thrombocytopenia and developed compensatory

Table 1. Haematological investigations.

Investigations	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day	8th day
Hemoglobin [*n*=11.5-14.5 g/dL]	15.1	14.6	15.5	13.9		13.2	13.3	12.8
Packed cell volume [PCV] [*n*=36% to 40%]	43.4	42.1	45.2	40.2		39	38	38
Total leucocyte count [*n*=4.0-12.0×10^9/L]	7.82		6.43					
Neutrophil [*n*=54%-62%]	82		69					
Lymphocyte [*n*=25%-33%]	13		26					
Monocyte [*n*=3%-7%]	4		4					
Easinophil [*n*=1%-3%]	0		0					
Basophil [*n*=0%-0.75%]	1		1					
C-reactive protein [CRP] [*n*=0.6-7.9 mg/L]	0	2.2		0.1				
Platelet count [*n*=150-400×10^9/L]	284	314	285	116	180	206	230	279

shock, and serum albumin was low (19 g/l); therefore, albumin infusion was given along with intravenous fluids according to the World Health Organization (WHO) guidelines. He had bilateral pleural effusion, gall bladder wall thickening and oedema with gross ascites, and the serology for dengue Non-Structural protein (NS1) antigen by ELISA was positive. His urine albumin was 3+ to 4+ since admission and had a nephrotic range of proteinuria. The gold standard to detect proteinuria is to measure total protein in urine over a 24-hour period time [7]. With these features, the child was diagnosed as a case of nephrotic syndrome complicated by dengue infection. Therefore, steroids were started on the 4th day, and after 6 days of steroids, his abdominal distension and scrotal oedema disappeared and his albumin was nil in the urine.

Proteinuria is one of the common abnormal findings detected by urine analysis in dengue infection, and few cases of heavy proteinuria (nephrotic range) have been reported [3–6]. Nephrotic-range proteinuria is defined as proteinuria >3.5 g/24 hours [2]. Dengue infection causing acute kidney injury is well documented [6]. Horvath et al. reported proteinuria in 74% of dengue patients, and out of them, only one elderly patient had nephrotic syndrome [8]. Self-limiting heavy proteinuria in the nephrotic range without other characteristics of nephrotic syndrome has been reported in dengue fever [3–6]. Protein excretion in urine of children with dengue increases during the course of dengue illness to reach a maximum level approximately 1 week after the onset of fever [7]. However, in this child, heavy proteinuria was present since the beginning of the illness. Even though nephrotic range proteinuria due to dengue infection was reported, none of them had other characteristic features of nephrotic syndrome such as scrotal oedema, classical onset of nephrotic syndrome or hyperlipidaemia as detected in our case. Puffiness is also known presentation in dengue illness, but generalised anasarca and scrotal oedema are characteristic features of nephrotic syndrome. Facial puffiness was observed in 63% of children with dengue infection in a study from south India [9].

Plasma leakage leading to dengue haemorrhagic fever (DHF) is the most dreadful complication

Table 2. Serology and other investigations.

Investigations	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day	8th day
Urine albumin	+++	++++	++++	++++	++++	++++	++++	+++
SGOT [*n*=15-50 U/L]	50	38	39	42		44		
SGPT [*n*= 5-45U/L]	20	15	14	16		27		
Serum bilirubin [*n*=<17µmol/L]		16.9						
Serum protiens [64-81g/L]		42						
Serum albumin [35-56 g/L]	19.4	21		22.9				24.4
Blood urea nitrogen [*n*=2.5-6.4 mmol/L]	25.34	35.7	23.5	19.9		11.4		9.9
Serum creatinine [*n*=19.4-52.2µmol/L]	61.8	61.8	61.8	61.8		61.8		61.8
Serum sodium [*n*=134-143 mmol/L]	138		136	136		135		134
Serum potassium [*n*=3.3-4.6 mmol/L]	6.6		4.5	4.3		4.8		4.3
24 hour urinary protein (mg/m^2/day)		21mg/m^2/d		106mg/m2/d				
ABG: pH [*n*=35-7.45] pCO2 [*n*=35-48 mmHg] pO2 [*n*=75-100mmHg] HCO3 [*n*=21-28 mmol/L]			7.27, 40, 80, 18		7.3, 40, 50, 22	7.4, 42, 64, 27		
Spot urinary protein to creatinine ratio	0.8	0.9						
Chest x-ray	Normal			Right pleural effusion	Bilatral pneumonia			Minimal right pleural effusion, clearence of infiltration

Total cholesterol 374 mg/dl [*n*= <170 mg/dl], triglycerides 299 mg/dl [*n*= <150 mg/dl], VLDL 59.8 mg/dl [*n*=2-30 mg/dl], HDL 41mg/dl [*n*=< 35 mg/dl], LDL 234 mg/dl [*n*=< 130 mg/dl]

ELISA for Dengue NS1 antigen positive, Weil-Felix and Widal test negative, Blood and urine culture sterile

Echocardiography normal

Sonography revealed odematous gall bladder and wall thickening of 6mm, bilateral kidneys showed raised cortical echotexture with intact corticomedullary differentiation; moderate ascites and bilateral pleural effusion.

ABG, arterial blood gases; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoproteins.

in dengue fever, and hypoproteinaemia usually indicates a plasma leakage [4,7]. Hypoalbuminaemia is a common feature in DHF [4]. As hypoalbuminaemia is a classical finding of nephrotic syndrome, it may confuse the treating clinician. Lai et al. reported dengue fever complicated by nephrotic syndrome in an adult [10]. However, this case is nephrotic syndrome child complicated by dengue infection.

The hypothesis of urinary protein excretion is the disruption of the glycocalyx of the endothelial cells either by direct action of the virus or the NS1 antigen causing plasma leakage [7]. The nephrotic-range proteinuria in DHF may be due to an autoimmune mechanism that the virus had triggered on the reticuloendothelial system, resulting in glomerulonephritis leading to glomerular leakage of protein [3].

CONCLUSION

Dengue infection may mimic nephrotic syndrome in clinical practice. As dengue infection is endemic in India, it can be associated with other illnesses such as nephrotic syndrome. Good history, thorough clinical examination and appropriate investigations, along with high index of suspicion, guide the clinician for the correct diagnosis.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

ETHICAL APPROVAL

Informed consent for participation and publication of medical details was obtained from the parents of the child. Confidentiality was ensured at all the stages. Ethics clearance and approval of the study were granted by JSS University Ethical Committee, Mysore.

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